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## ABSTRACT

The present invention relates PI3K crystals, polypeptide muteins, polypeptide fragments, antibodies thereto, nucleic acids coding for these polypeptides, methods of modifying PI3Kγ activity, and methods of modulating PI3Kγ activity. These include polypeptides and methods thereof, relating to, e.g., phospholipid binding, lipid kinase activity, modulating Ras activity in activating the PI3Kγ, binding of PI3Kγ to cell membranes, and modulating protein-protein interactions with PI3Kγ.